COMMISSION ON HUMAN MEDICINES (CHM)
COVID-19 VACCINES BENEFIT RISK EXPERT WORKING GROUP

Minutes of the meeting held on **Tuesday 19th October 2021** at **14:30** via videoconference

Participants Present

Members

Professor Sir M Pirmohamed (Chair)
Professor J Breuer
Mr VI G Fenton-May
Professor N French
Professor D Goldblatt
Ms S Hunneyball
Professor K Hyrich
Professor P J Lehner
Dr S Misbah
Professor Y Perrie[1]
Professor S Price
Professor K M G Taylor
Dr R Thorpe[1]
Professor S Walsh
Mrs M Wang

Apologies

Professor G Dougan
Sir M Jacobs
Professor H J Lachmann
Mr R Lowe
Dr A Riordan
Professor C Robertson
Professor T Solomon
Professor M Turner
Professor C Weir

Invited Experts[2]

[redacted]

Visiting Experts[3]

[redacted]

Observers

[redacted]

Professional Staff of MHRA Present

Principal Assessors

[redacted] - LD
[redacted] - VRMM

Presenters supporting specific items[4]

[redacted] – VRMM

MHRA Observers

[redacted] VRMM
[redacted]nforth - VRMM
[redacted] - VRMM
[redacted] – MHRA Policy
[redacted] - VRMM
[redacted] – VRMM
[redacted] - VRMM
[redacted] – VRMM
[redacted] - LD
[redacted] – VRMM
[redacted] - VRMM

Secretariats

[redacted]

[redacted]

13th April 2022

Key

LD = Licensing Division
VRMM = Vigilance & Risk Management of Medicines
NIBSC = National Institute for Biological Standards & Control
Directorate = Director of Operational Transformation

[1] joined during item 2
[2] participated for items 2 & 3
[3] participated for item 2 only
[4] supported specific items

1. Introduction and Announcement

1.1 The Chair reminded Members, invited Experts and observers that the content of papers and proceeding of the meeting are strictly confidential and should be treated as 'Official – sensitive commercial' and should not be disclosed. There is no consent for members / participants to record the meeting, take screenshots or photographs of presentations. The meeting was recorded by the MHRA Secretariat for minute taking purposes only. The Chair & Members including all participants gave full consent to the recording prior to the start of the meeting.

1.2 Conflict of Interest Policy (Annex I to the minutes)

The Chair reminded members and participants that, in accordance with the CHM Code of Practice, they should declare any financial interests (personal or non-personal, specific or non-specific) which they have, or which an immediate family member has, in any of the agenda items. Members were also reminded to declare any other matter which could reasonably be perceived as affecting their impartiality.

1.3 Participants declared interests and other relevant interests for this meeting listed at **Annex II** to the minutes.

1.4 Apologies were received from Professors Dougan, Lachmann, Robertson, Solomon, Turner, Weir, Dr Riordan, Mr Lowe and Sir Michael Jacobs for this meeting.

1.5 The Chair welcomed the following visiting/invited experts:

[redacted] University of Cambridge

[redacted]
Swedish PRAC Delegate

[redacted]
Swedish Medical Products Agency

[redacted]

[redacted] Bristol Heart Institute

1.6 The Chair welcomed the following observers:

[redacted]
Public Health Scotland

[redacted]
UK Health Security Agency

[redacted]
NHS England and NHS Improvement (National)

2. Nordic cohort: preliminary results SARS-CoV-2 vaccination and myocarditis

2.1 The Nordic cohort study includes all individuals over 12 years of age eligible for vaccination in Denmark, Finland, Norway, and Sweden and examines the 28-day risk window following first and second vaccination with Pfizer, Moderna or AstraZeneca vaccines in homologous or heterologous schedules. The outcome event studied was myocarditis or pericarditis with hospital-based diagnosis or inpatient hospitalisation. The EWG was informed of covariates and details of the metanalysis.

3. Update - COVID-19 vaccines and myo/pericarditis

3.1 The EWG were presented with an update on Yellow Card reports of myocarditis and pericarditis with the three COVID-19 vaccines in use in the UK vaccination programme as well as new information from company data, international data and literature.

3.2 The EWG were informed that reporting rates remained similar between the first and second dose of the Pfizer/BioNTech vaccine and the reporting rate for second dose Pfizer/BioNTech in the under 18 age group had decreased. The Moderna vaccine had higher reporting after the second dose in the younger age groups and a higher reporting rate when compared to the Pfizer/BioNTech vaccine. The EWG heard that for the AstraZeneca vaccine, the reporting rates were overall lower than for both of the mRNA vaccines.

3.3 The EWG heard that the nature of the Yellow Card reports was similar to that previously presented for the vaccines, with higher proportions of reports in males and in younger age groups. The reports for the mRNA vaccines were seen in younger age groups compared with the AstraZeneca vaccine. The EWG heard that some reports of myocarditis and pericarditis following booster doses had been received, with the average age higher than seen for the primary doses but with no indication of these reports being more severe.

3.4 The EWG were presented with data from a review of myocarditis and pericarditis by Moderna that included a review of their paediatric study, which did not identify any reports of myocarditis or pericarditis. The company had updated their ongoing safety studies to ensure data on myocarditis and pericarditis was captured.

3.5 The EWG heard information on the reporting rates for the Janssen vaccine from company and international data, with higher reporting seen in younger age groups, but similar to the rates seen with the AstraZeneca Yellow Card data. The EWG considered this vaccine should continue to be monitored for these events.

3.6 The EWG were presented with data from the Edinburgh study, which showed an increased risk of myocarditis with both first and second doses for Pfizer/BioNTech and Moderna vaccines as well as for the first dose of AstraZeneca vaccine. It was stated that in data stratified to under 40 years the incidence rate ratio was higher for Moderna compared to both AstraZeneca and Pfizer vaccines or for subjects with a positive SARS-CoV-2 test, although with overlapping confidence intervals between the estimates. The EWG noted that the study found that in the overall analysis, there was a much greater risk of myocarditis and pericarditis in the month post SARS-CoV-2 infection. The EWG commented on the limitation of analysis in younger age groups due to small numbers and that further data on this would be helpful for consideration when available.

3.7 The EWG were presented with new data that had been identified from international regulators, which followed a similar pattern of more frequent reporting in younger ages and males following the second dose. The EWG noted that a higher reporting rate with the Moderna vaccine in comparison to the Pfizer/BioNTech vaccine, particularly after second dose, was being seen in the international data.

3.8 The EWG considered that while there may be a slightly higher risk for Moderna in the younger population compared to Pfizer/BioNTech in international data, the UK data did not currently show a clear difference and there was currently not enough evidence to recommend Moderna should not be given in any particular age group. The EWG considered further data were required and the MHRA should continue to monitor this and regulatory action could be considered if further data supporting this should become available. The EWG noted that public health bodies had made changes to vaccine preference in their countries but that no regulatory action had been taken by regulatory bodies.

3.9 The EWG concluded that the benefits still exceeded the risks overall for each vaccine and for all authorised subpopulations. No regulatory action was required based on the data presented.

4. Bell's Palsy and COVID-19 vaccines: A CPRD study

4.1 The MHRA presented the results of a CPRD based self-controlled case-series (SCCS) study where no association between COVID-19 vaccines and an increased risk of Bell's Palsy was detected.

4.2 The MHRA also gave an overview of the OpenSAFELY study that investigates the risk of Bell's Palsy following exposure to COVID-19 vaccines using a different SCCS study design and other UK-based data sources. The EWG noted that joint interpretation of the two parallel studies would provide a fuller picture of the true risk of Bell's Palsy in association with COVID-19 vaccines.

4.3 The EWG concluded that no regulatory action is required based on the current findings.

5. <u>Future Steps / Any Other Business</u>

None.

6. <u>Date and time of next meeting</u>

The next scheduled meeting is to take place on **Friday 29th October** at **14:30**.

The Meeting today started at 14:31 and ended at 16:12.

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Annex I

Conflict of Interest Policy for CHM COVID-19 Vaccine Benefit Risk EWG

Chair and Members

- May not hold current personal interests in one or more companies associated with the development of COVID-19 vaccines
- May not currently be or have previously been involved in the development of COVID-19 vaccines

Invited to all meetings, receives all papers and presentations and is permitted full participation in discussion, including drawing up conclusions and recommendations

Invited experts

- May hold current personal interests in one or more companies associated with the development of COVID-19 vaccines
- May currently be or have previously been involved in the development of COVID-19 vaccines

May be invited to all relevant meetings, receives all papers and presentations and is permitted to participate in discussions when invited by the Chair. Does not contribute to conclusions and recommendations

Observers

Are invited to attend all meetings. Will not participate in drawing up conclusions and recommendations.

Annex II

The following participants declared interests and other relevant interests at the meeting today:

Professor Sir Munir Pirmohamed - NPNS AstraZeneca - Research grant to UOL to support PhD in drug interactions.
Other relevant interests in Pfizer, Janssen, Sanofi – Sir Munir is part of an EU-funded IMI consortium on gene therapy, and these companies are partners in the project. The University of Liverpool will get funding from the EU (but not from the partners), this IMI project commences on 3rd November 2020.
AGILE – this is a Liverpool early phase trial platform (between University of Liverpool and Liverpool School of Tropical Medicine). It is funded by the Wellcome Trust and UKRI/DHSC/NIHR. It is NOT evaluating vaccines, but only drugs to treat COVID-19. Sir Munir is not on the trial management group, and he is not directly involved in choosing the compounds for the study. Sir Munir has no involvement with any of the developers of the compounds to be studied (academic or industrial).
Sir Munir is a member of the UK COVID Therapeutics Advisory Panel (UK-CTAP), which is advising the CMO on which compounds need to be prioritised for the RECOVERY+ trial (RECOVERY is funded via NIHR/DHSC).

Professor Breuer– NPNS – Professor Breuer is on the data safety monitoring committee, DSMB, a study looking at combining vaccines being run by Matthew Snape in Oxford. There does not appear to be any involvement of the vaccine manufacturers and is for already licensed vaccines. The study is funded by the NIHR (Dec 2020).

Professor French - Other relevant interest - Provides clinical care when in covering the acute medical wards where patients with COVID-19 are cared. NPNS in GSK - In September 2020 a sub-contract was signed with the Liverpool School of Tropical Medicine to undertake work evaluating the safety and effectiveness of GSK's RTS's malaria vaccine in Malawi. GSK are the primary funders to the LSTM.

Ms Hunneyball - Other relevant interest – writes articles published in the Chemist and Druggist magazine, a trade magazine for pharmacists, but receives no payment for these articles. The information referred to in the articles is in the public domain. Ms Hunneyball makes it clear that these are her personal views and reflections and references all sources of information used.

Professor Hyrich – NPNS - Professor Hyrich was co-I on an investigator-initiated research grant exploring predictors of outcome in rheumatoid arthritis. NPNS Pfizer- she is a Co-I on a grant exploring adherence to JAK inhibitors in rheumatoid arthritis. NPNS in Abbvie, Professor Hyrich gave some lectures at an education conference on effectiveness of treatment for rheumatoid arthritis.

Professor Lehner - Other relevant interest – Professor Lehner previously held a DPAC (Discovery Partnership with Academia) agreement with GSK, but this has been completed. Professor Lehner's participation in his local hospital D and T governance committee deliberations would form the normal activity and professional responsibility in his post and does not interfere with the EWG considerations (Sept 2020).

Dr Misbah - NPNS - Holds honorary Senior Lectureship with University of Oxford & Oxford University Hospitals NHS Foundation Trust.

Professor Perrie - NPNS in Pfizer & AstraZeneca arising from a contract for a grant (March 2018), which includes contributions from these companies to the University of Strathclyde, Janssen in writing a grant for a PhD (now funded), GSK – arising from an EU grant to University of Strathclyde (Jan 2019-Dec 2019).

Professor Price - NPNS in GSK and AstraZeneca – which relates to donations provided by both companies to the British Toxicology Society (BTS) to support their Annual Congress and Education and Training of which Professor Price is currently President of the Society (2020-2022).

Mrs Wang – Other relevant interests arising from being highly sensitive to insect stings, and plant products such as Hyacinth bulbs, as recorded on Mrs Wang's medical records. The family of Mrs Wang lives with several rare diseases and conditions, some of which result in epileptic fits.

Observers

[redacted] - Lapsed and NPNS - Regarding companies to declare interests for, prior to joining Public Health Scotland, [redacted] worked for a company that provided epidemiological services to the pharmaceutical industry. Whilst working there, [redacted] supported respiratory vaccine development activities at [redacted] has now left that role.

[redacted] – Other relevant interest in Pfizer & GSK. The Immunisation and Countermeasures Division has provided vaccine manufacturers (including Pfizer and GSK) with post-marketing surveillance reports on pneumococcal and meningococcal infection which the companies are required to submit to the UK Licensing authority in compliance with their Risk Management Strategy. A cost recovery charge is made for these reports.